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CONTRACT NO DA-CRD AG-892-544-65-816.

INCLUSIVE DATES 24 July 1963 TO 31 December 1963

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SUBJECT OF INVESTIGATION

⑥ AUTOMATIC RECORDING OF PO_2 , PCO_2 , PH,

Na AND K IN THE BLOOD AND THE BRAIN,

RESPONSIBLE INVESTIGATOR

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SECTION I

During the period from July 24 1963 to December 31 1963, studies were made partly on Phase 1 and partly on Phase 2 of the services stated in the application for consideration of research project dated April 20 1963.

1. Establishment and reexamination of the electrodes for continuous recording of PO_2 and respiration.

Recently 8 or 9 parameters such as brain surface temperature (thought to be cerebral blood flow), brain PO_2 , PCO_2 , pH, sodium ionic activity, systemic blood pressure, EEG, EKG and respiration were recorded on a graph with 8 channel polygraph. The details of the construction and specification of the electrodes of PO_2 , PCO_2 , pH, Na^+ and thermistor were already described on the final report of last year (Contract No. DA-92-557-FEC-35889).

a. Reexamination of the sensitivity of PO_2 electrode. We went to Sapporo to see the Research Institute of Applied Electricity attached to Hokkaido University and obtained some fundamental information about the polarographic method for measurement of oxygen tension. According to Dr. Mochizuki who is a chief of Department of Physiology of the Research Institute of Applied Electricity, the pH and concentration of saline which is trapped inside the polyethylene membrane has influence on the sensitivity of PO_2 electrode. We examined that of our PO_2 electrodes with saline of 0.9, 7.2 per cent and saturation in concentration and 0.9% saline of 5.0, 7.5 and 9.0 in pH, respectively. However, no definite relationship of pH and concentration of saline with the sensitivity of PO_2 electrode was obtained.

b. Continuous recording of respiration. Respiration was recorded by means of thermistor which was commercially available. There is no doubt that thermistor can represent the frequency of respiration, when thermistor is put on the way of the inspired and expired air. Because the temperature of expired air is higher than that of inspired air and the difference of air temperature reflects on the change of resistance of thermistor. Thermistor was wired into one arm of a Wheatstone's bridge, the output of which was connected to the input of one channel of a polygraph. The heat capacity of thermistor must be small enough for recording of respiration.

However, there are some problems on recording of respiration volume by means of thermistor. Recordings of respiration were examined in the different position of thermistor. Animal experiments were usually performed in the controlled respiration with a respirator, however, sometimes in the spontaneous breathing without it, so the recordings of respiration were examined both with and without respirator.

- (1) Controlled respiration with respirator. Tracheal cannula, which was a T-tube made of glass and put in the cat's trachea, was connected to a respirator with plastic tube, and frequency and volume of respiration were controlled by respirator.

- (a) Frequency of respiration. Frequency of respiration could be correctly recorded on a graph as expected.
- (b) Volume of respiration. Influence of the position of thermistor was examined. However, there could not be found any correlation between the position of thermistor in depth or sectional plane of the cannula and the amplitude of recording of respiration volume.

Correlation of the respiration volume given by a respirator with the amplitude of recording on a graph was examined in the different position of the thermistor. One thermistor was put in the position of 4 cm. in depth from the outer orifice of the tracheal cannula and another 7 cm. in depth. Respirator was controlled to give a certain volume and double of that to the animal. Regarding to the reproducibility and linearity in correlation, the thermistor which was put deeper in 7 cm. appeared to be better than that in 4 cm. Then, one thermistor was put in the center of the tube and another in the periphery, and the respirator was controlled to give various volumes. No difference was observed in the different position of the thermistor, and the linear relationship in a strict sense between the respiration volume and the amplitude of recording could not be obtained, however, the amplitude became larger when the larger respiration volume was administered.

- (2) Spontaneous breathing without respirator. Thermistor was put in the various parts both in depth and section and the continuous recording of respiration was observed. Amplitude of respiration curve showed some changes when the position of thermistor was changed, however, no definite correlation between them could be observed. But the constant recording of respiration could be obtained if the thermistor was fixed in a certain position.

2. Application of the electrodes to the cat brain.

Cats weighing 3 - 4 Kg. were used for experiments. Under general anesthesia with ether or nembutal, the femoral vein and artery were exposed and polyethylene catheters were inserted into each of them for administration of drugs and connecting to the electromanometer respectively. Tracheostomy was performed for connecting to the respirator or inhalation of gas mixture. Then cat was fixed by use of a head holder and a craniectomy was performed over one hemisphere. After incising the dura, electrodes of PO_2 , PCO_2 , pH, Na^+ , EEG and thermistor were placed on the pial surface of the brain with a light contact.

a. Anoxia.

- (1) Asphyxia. Asphyxiation was induced by turning off the mechanical respirator or clamping of the rubber tubing of the air way in the case of spontaneous breathing. As

respiration ceased, cortical PO_2 decreased and EEG slowing appeared when cortical PO_2 decreased below some level. Blood pressure rose during the first phase of medullary anoxia and cortical blood flow increased because of rise in blood pressure and PCO_2 and decrease in PO_2 . Cortical PCO_2 increased accompanied by decrease in pH and sodium ionic activity.

- (2) Pure nitrogen gas breathing. Anoxia was also induced by breathing 100% nitrogen and produced changes similar to those seen with asphyxia. Brain oxygen tension decreased and ~~EEG slowing appeared, and cortical blood flow decreased,~~ occasionally with initial increase. Cortical PCO_2 initially decreased and then increased, cortical pH often decreased despite reduced cortical PCO_2 . Sodium ionic activity showed decrease. Blood pressure showed decrease with an initial increase.

b. Effect of chlordiazepoxide on cerebral circulation and metabolism of normal cats. Effects of chlordiazepoxide on the cerebral circulation and metabolism were reported by use of nitrous oxide method or separated brain perfusion method. So this effect was examined here by our method.

Chlordiazepoxide of 2, 3, and 4 mg./Kg. was respectively administered and 8 experiments were performed. Blood pressure showed decrease: ~~in some cases~~ it decreased only for the first several minutes and in other cases decreased blood pressure maintained for more than ten minutes. Cortical blood flow showed a tendency to decrease, corresponding to the fall of blood pressure. A few cases showed decrease in PO_2 , however, some cases showed no appreciable change, and tendency to decrease in PCO_2 was not so dominant as in T and blood pressure. PCO_2 showed decrease and pH increase. Sodium ionic activity showed slight decrease in some cases and temporary decrease followed by increase in some cases. All experiments on this subject were performed under the controlled respiration with respirator.

SECTION II

Contemplated research activity for the next period of half year

The establishment of the electrodes and method for continuous recording of: brain temperature, PO_2 , $PCCO_2$, pH, sodium ionic activity, blood pressure, EEG, ERG and respiration has almost been accomplished. So, in the next period, the application of the electrodes to the cat brain will be main subject. Effect of chlordiazepoxide on the cerebral circulation and metabolism of normal cats were already obtained, so effect of it on the animals previously given megimide will be observed. And then, effect of metabolic inhibitors such as malonate, moniodoacetate and dinitrophenol will be observed by means of our new technique, and comparison of the effect obtained from this technique with that obtained from Warburg's manometrics, which we formed several years ago, will be made.